

## **Topics/Questions for Discussion for SPL ER/DL Process Team – 20-Sept-17**

### **UPCOMING EVENTS**

**October 4<sup>th</sup>** SPL Process Team Meeting: Speakers Leyla.Rahjou-Esfandiary and Paul Loebach on Drug Certification Requirements

**October 5** The FDA is holding a free meeting on Electronic Drug Registration & Listing Using CDER Direct.

<https://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm572869.htm>

**November 1 & 2** CDER Prescription Drug Labeling Conference 2017

[https://events-na12.adobeconnect.com/content/connect/c1/1315899612/en/events/event/shared/1760150377/event\\_registration.html?sco-id=1760179387&\\_charset=utf-8](https://events-na12.adobeconnect.com/content/connect/c1/1315899612/en/events/event/shared/1760150377/event_registration.html?sco-id=1760179387&_charset=utf-8)

**SPL Work Group Wiki page:**

<http://spl-work-group.wikispaces.com/>

### **Drug Listing Presentation – Ben Harpster**

*Please note that this discussion is based on GSK procedures. Please review the Establishment Registration and Drug Listing Guidance or contact eDRLS with drug listing issues.*

#### **Why Drug Listing is Important**

- Compliance – Drug listings must be submitted within 14 days of FDA approvals.
- Uploads product information to FDA websites such as the NDC Directory (<https://www.fda.gov/Drugs/InformationOnDrugs/ucm142438.htm> ) and the NSDE (<https://www.fda.gov/forindustry/datastandards/structuredproductlabeling/ucm240580.htm> ). Much of it also is found on NIH's DailyMed (<https://dailymed.nlm.nih.gov/dailymed/index.cfm> ). This information is extracted by some down stream systems such as product ordering systems.
- Facilitates importation of product into the U.S. This is the topic for today.

#### **What Happened?**

- Several years ago, GSK noticed a big uptick in FDA holds on CDER products.
- The FDA Compliance officers at the ports of entry that we shipped our product thru were informing us that our products were not drug listed.
- At that time, all of GSK's products had what I call the distributor drug listing (uses the marketed NDC) in place with full supply chain information from API Manufacturer to Label. So the statement that our products were not drug listed did not make any sense.
- After numerous calls with the FDA Compliance officers we found out that their internal database was not showing the supply chain information found in the distributor drug listing. They did not understand how that information got there, they just knew that they were required to see it to release a product.

- Thru future discussions with the FDA and trial and error, we came to realize that the single distributor drug listing was no longer enough. We needed several drug listings to support importation, regardless of whether we made the product ourselves, or it was made by a CMO.

Example of what GSK was doing:

- Single drug listing.
- Contained full supply chain information
  - API Manufacturer
  - Manufacturer
  - Analysis
  - Pack
  - Label
- The NDCs from the single drug listing were the only NDCs provided at time of import.

#### **What GSK is doing now**

- 3 drug listings (either by myself, or with the help of third parties). They are API Bulk, Manufacturer, and Distributer.
- 3 NDCs can be provided for importation.
- The Distributer drug listing still contains the full supply chain.

#### **Drug Listing Requirements for Importation**

##### **API Bulk Drug Listing**

- Drug Listing must be active and current at time of Import.
- NDC must contain a labeler code specific to the manufacturer or an affiliate.
- That NDC should be provided as part of the import information.

##### **Manufacturer Bulk Drug Listing**

- Drug listing must be active and current at time of import.
- NDC must contain a labeler code specific to the manufacturing site or a affiliate.
- That NDC should be provided as part of the import information.

##### **Distributor Drug Listing**

- Drug listing must be active and current at time of import.
- NDC must contain a labeler code specific to the distributor or an affiliate.
- Can be done by either the manufacturer or the distributing company.
- That NDC must be provided as part of the import information for finished /packaged goods.

#### **Why are all of these drug listings needed?**

- Regulations require it.

#### §207.41 Who must list drugs and what drugs must they list?

(a) Each registrant must list each drug that it manufactures, repacks, relabels, or salvages for commercial distribution. Each domestic registrant must list each such drug regardless of whether the drug enters interstate commerce. When operations are conducted at more than one establishment, and common ownership and control exists among all the establishments, the parent, subsidiary, or affiliate company may submit listing information for any drug manufactured, repacked, relabeled, or salvaged at any such establishment. A drug manufactured, repacked, or relabeled for private label distribution must be listed in accordance with paragraph (c) of this section.

(b) Registrants must provide listing information for each drug in accordance with the listing requirements described in §§207.49, 207.53, and 207.54 that correspond to the activity or activities they engage in for that drug.

(c)(1) For both animal and human drugs, each registrant must list each drug it manufactures, repacks, or relabels for commercial distribution under the trade name or label of a private label distributor using an NDC that includes such private label distributor's labeler code.

(2) Additionally, in the case of human drugs, each registrant must list each human drug it manufactures, repacks, or relabels using an NDC that includes the registrant's own labeler code, regardless of whether the drug is commercially distributed under the registrant's own label or trade name or under the label or trade name of a private label distributor.

- (Comment 21) One comment requested guidance regarding the information needed for “active drug substance manufacturers” to register and list.
- (Response) In this final rule, the term “active pharmaceutical ingredient” (API) is defined in § 207.1. The registration obligation applies to each domestic establishment that manufactures, repacks, relabels, or salvages a drug or an animal feed bearing or containing a new animal drug (whether or not that product is commercially distributed). It also applies to each foreign establishment that manufactures, repacks, relabels, or salvages a drug or an animal feed bearing or containing a new animal drug that is imported or offered for import into the United States. ***In each case, the term “drug” includes: (1) An API by itself, (2) an API that has been combined with one or more other APIs or inactive ingredients (see definition of “unfinished drug” in § 207.1), and (3) finished drug products (see definition of “finished drug product” in § 207.1).***
- This is found in <https://www.federalregister.gov/documents/2016/08/31/2016-20471/requirements-for-foreign-and-domestic-establishment-registration-and-listing-for-human-drugs>
- This is how the information gets into the database that the FDA compliance officers at the various ports of entry utilize to release a product.
  - The single distribution drug listing that some were doing does not populate all the needed columns in the database.
- This is also one of the ways that the FDA can verify that a manufacturer is aware that it is making a product for the U.S. market (more a concern for monograph products and API).

- Additionally, for API, this is one way that the FDA makes sure that they are aware of a facility for inspection purposes.

### **What is needed to populate the FDA database?**

#### *Currently, for API Manufacturing*

- A “bulk ingredient” file has to be filled out. In the Product Data Elements Section, in the Market Information for Category, Bulk Ingredient must be chosen.

#### *For the manufacturer drug listing*

- A “bulk ingredient” file has to be filled out. In the Product Data Elements Section, in the Market information for Category, Drug for further processing must be chosen.
- One of the finished product templates can be filled out.

#### For OTC products

- use either Human OTC Drug Label or Human OTC Drug Label with Highlights. In marketing Information, for the Category choose OTC Monograph Drug Product Manufactured Exclusively for Private Label Distributor.

#### For Pharma products

- use either Human Prescription Drug Label or Human Prescription Drug Label with Highlights. In marketing Information, for the Category choose Approved Drug Product Manufactured Exclusively for Private Label Distributor.

#### *For the distributor drug listings:*

- Fill out the appropriate finished product template.